
Modifying the Mitochondrial Genome.

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Public Summary:

Human mitochondria produce ATP and metabolites to support development and maintain cellular homeostasis. Mitochondria harbor multiple copies of a maternally inherited, non-nuclear genome (mtDNA) that encodes for 13 subunit proteins of the respiratory chain. Mutations in mtDNA occur mainly in the 24 non-coding genes, with specific mutations implicated in early death, neuromuscular and neurodegenerative diseases, cancer, and diabetes. A significant barrier to new insights in mitochondrial biology and clinical applications for mtDNA disorders is our general inability to manipulate the mtDNA sequence. Microinjection, cytoplasmic fusion, nucleic acid import strategies, targeted endonucleases, and newer approaches, which include the transfer of genomic DNA, somatic cell reprogramming, and a photothermal nanoblade, attempt to change the mtDNA sequence in target cells with varying efficiencies and limitations. Here, we discuss the current state of manipulating mammalian mtDNA and provide an outlook for mitochondrial reverse genetics, which could further enable mitochondrial research and therapies for mtDNA diseases.

Scientific Abstract:

Human mitochondria produce ATP and metabolites to support development and maintain cellular homeostasis. Mitochondria harbor multiple copies of a maternally inherited, non-nuclear genome (mtDNA) that encodes for 13 subunit proteins of the respiratory chain. Mutations in mtDNA occur mainly in the 24 non-coding genes, with specific mutations implicated in early death, neuromuscular and neurodegenerative diseases, cancer, and diabetes. A significant barrier to new insights in mitochondrial biology and clinical applications for mtDNA disorders is our general inability to manipulate the mtDNA sequence. Microinjection, cytoplasmic fusion, nucleic acid import strategies, targeted endonucleases, and newer approaches, which include the transfer of genomic DNA, somatic cell reprogramming, and a photothermal nanoblade, attempt to change the mtDNA sequence in target cells with varying efficiencies and limitations. Here, we discuss the current state of manipulating mammalian mtDNA and provide an outlook for mitochondrial reverse genetics, which could further enable mitochondrial research and therapies for mtDNA diseases.

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